

WHAT IS CLAIMED IS:

1. A synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a human HER2/neu protein as set forth in SEQ ID NO:2, the synthetic nucleic acid molecule being codon-optimized for high level expression in a human cell.
2. The synthetic nucleic acid molecule of claim 1 wherein the sequence of nucleotides comprises the sequence of nucleotides set forth in SEQ ID NO:1.
3. A vector comprising the nucleic acid molecule of claim 1.
4. A host cell comprising the vector of claim 3.
5. A synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a variant human HER2/neu polypeptide that has at least 90% identity to the amino acid sequence of SEQ ID NO:2, which may include up to N_a amino acid alterations over the entire length of SEQ ID NO:2, wherein N_a is the maximum number of amino acid alterations, and is calculated by the formula
$$N_a = X_a - (X_a Y),$$
in which X_a is the total number of amino acids in SEQ ID NO:2, and Y has a value of 0.90, wherein any non-integer product of X_a and Y is rounded to the nearest integer prior to subtracting such product from X_a , wherein the sequence of nucleotides is codon-optimized for high level expression in a human cell.
6. A synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a human HER2ECDTM protein as set forth in SEQ ID NO:14, the synthetic nucleic acid molecule being codon-optimized for high level expression in a human cell.
7. The synthetic nucleic acid molecule of claim 6 wherein the sequence of nucleotides comprises the sequence of nucleotides set forth in SEQ ID NO:9.
8. A vector comprising the nucleic acid molecule of claim 6.
9. A host cell comprising the vector of claim 8.
10. A synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a variant human HER2ECDTM polypeptide that has at least 90% identity to the amino acid

sequence of SEQ ID NO:14, which may include up to N_a amino acid alterations over the entire length of SEQ ID NO:14, wherein N_a is the maximum number of amino acid alterations, and is calculated by the formula

$$N_a = X_a - (X_a Y),$$

- 5 in which X_a is the total number of amino acids in SEQ ID NO:14, and Y has a value of 0.90, wherein any non-integer product of X_a and Y is rounded to the nearest integer prior to subtracting such product from X_a , wherein the sequence of nucleotides is codon-optimized for high level expression in a human cell.

10 11. A process for expressing a human HER2/neu protein in a recombinant host cell, comprising:

- (a) introducing a vector comprising the nucleic acid of claim 1 into a suitable host cell; and,
- (b) culturing the host cell under conditions which allow expression of said human HER2 protein.

15 12. A process for expressing a human HER2ECDTM protein in a recombinant host cell, comprising:

- (a) introducing a vector comprising the nucleic acid of claim 6 into a suitable host cell; and,
- 20 (b) culturing the host cell under conditions which allow expression of said human HER2ECDTM protein.

25 13. A method of preventing or treating HER2-associated cancer comprising administering to a mammal a vaccine vector comprising a synthetic codon-optimized nucleic acid molecule, the nucleic acid molecule comprising a sequence of nucleotides that encodes a human HER2/neu protein as set forth in SEQ ID NO:2 or a human HER2ECDTM protein as set forth in SEQ ID NO:14.

30 14. A method according to claim 13 wherein the mammal is human.

15. A method according to claim 14 wherein the vector is an adenovirus vector or a plasmid vector.

16. A method according to claim 15 wherein the vector is an adenoviral vector comprising an adenoviral genome with a deletion in the adenovirus E1 region, and an insert in the adenovirus E1 region, wherein the insert comprises an expression cassette comprising:

- 5 (a) a codon-optimized polynucleotide encoding a human HER2 protein or a human HER2ECDTM protein; and
(b) a promoter operably linked to the polynucleotide.

17. A method according to claim 15 wherein the vector is a plasmid vaccine vector, which comprises a plasmid portion and an expressible cassette comprising:

- 10 (a) a codon-optimized polynucleotide encoding a human HER2 protein or a human HER2ECDTM protein; and
(b) a promoter operably linked to the polynucleotide.

18. An adenovirus vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

- 15 (a) a codon-optimized polynucleotide encoding a human HER2 protein or encoding a human HER2ECDTM protein; and
(b) a promoter operably linked to the polynucleotide.

19. An adenovirus vector according to claim 18 which is an Ad 5 vector.

20. An adenovirus vector according to claim 18 which is an Ad 6 vector or an Ad 24 vector.

21. A vaccine plasmid comprising a plasmid portion and an expression cassette portion, the expression cassette portion comprising:

- 25 (a) a codon-optimized polynucleotide encoding a human HER2 protein or a human HER2ECDTM protein; and
(b) a promoter operably linked to the polynucleotide.

22. A method of treating a mammal suffering from HER2-associated cancer comprising:

- (a) introducing into the mammal a first vector comprising:

i) a codon-optimized polynucleotide encoding a human HER2 protein or a human HER2ECDTM protein; and

ii) a promoter operably linked to the polynucleotide;

(b) allowing a predetermined amount of time to pass; and

5 (c) introducing into the mammal a second vector comprising:

i) a codon-optimized polynucleotide encoding a human HER2 protein or a human HER2ECDTM protein; and

ii) a promoter operably linked to the polynucleotide.

10 23. A method according to claim 22 wherein the first vector is a plasmid and the second vector is an adenovirus vector.

24. A method according to claim 22 wherein the first vector is an adenovirus vector and the second vector is a plasmid.

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